Why did RAS inhibition not accelerate regression in the RELIEF-AS study (1)? First, the magnitude of afterload reduction by surgical aortic valve replacement may swamp any signal: mean valve gradients decreased from 48 ± 16 mm Hg to 12 ± 6 mm Hg with 19% LVM regression at 1 year, compared with the LVM regression in the RIAS trial (2) of 2.5% at 1 year (or 5.4% compared with their placebo control group). Second, although RAS inhibition reduces LVH across various diseases (the majority of evidence is in arterial hypertension), aortic stenosis is different: the pressure drop is pre-coronary, and there are clear differences in the myocardial changes in aortic stenosis compared with those in hypertension (3). Third, LVH needs to be considered in context. Not all LVH is bad: few would consider the physiological hypertrophy of athletes (predominantly cellular hypertrophy) as a potential drug target, and in moderate aortic stenosis (the RIAS study), at least some of the LVH may have been appropriate (4). The imaging techniques used in RELIEF-AS in differentiating cellular and matrix responses within LVH may offer us new understanding. At this time, we do not know the relative effects of different drugs on myocyte hypertrophy versus interstitial expansion; future care may deliver personalized medicine approaches based on the precise type and context of any LVH to maximize outcome improvement.

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Revascularization Strategies in Patients With Acute MI and Cardiogenic Shock

In a recent issue of the *Journal*, Lee et al. (1) present data based on the Korea Acute Myocardial Infarction Registry (KAMIR)-National Institutes of Health registry and conclude that multivessel percutaneous coronary intervention (PCI) is associated with a lower risk of death in ST-segment elevation myocardial infarction and cardiogenic shock (CS) compared with infarct-related-artery (IRA)-only PCI.

We believe that the following points warrant more detailed discussion:

- It remains unclear if and how patients were prospectively assigned to multivessel PCI. For example, patients in whom death occurred before staged procedures seem to have been included in the IRA-only PCI group. Statistical adjustment for this confounder is not possible. This factor could be a major trigger for the higher mortality after IRA-only PCI.
- The reported 1-year mortality (27%) and the rate of renal replacement therapy at 30 days (3%) are extremely low for a CS cohort.
- There have been recent reports on the current topic based on the KAMIR registry (2,3). The findings are inconsistent despite overlapping patient inclusion, similar definitions, and comparable baseline characteristics, which could be indicative of unknown confounders triggering the differing results.
- The CULPRIT-SHOCK (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) trial showed superiority of culprit-lesion-only PCI with the option of staged revascularization over immediate multivessel PCI with respect to all-cause mortality (4). The authors repeatedly state that "…patients with CS were excluded in all randomized trials…"; this statement is misleading. Furthermore, in the present analysis (1), 40% of the so-called multivessel PCI group underwent staged procedures. This total reflects the IRA-only PCI with possible staged revascularization arm of the CULPRIT-SHOCK

trial. It seems desirable to uniformly report revascularization strategies, given the findings of the CULPRIT-SHOCK trial, to allow a true comparison of the results and subsequently support evidence-driven decision-making.

- The prevalence of chronic total occlusion (CTO) in CS is high. Hence, approximately one-quarter of patients (23%) enrolled in the CULPRIT-SHOCK trial presented with CTO (4). Immediate recanalization was attempted in 51% of patients in the immediate multivessel PCI group and was successful in 30%. There was no influence of CTO presence on the primary study endpoint (p value for interaction 0.26). Lee et al. (1) correctly state that this is an important aspect of the CULPRIT-SHOCK trial. Consequently, this topic will be further elucidated in a dedicated subanalysis. Regrettably, the present paper does not include data on the prevalence or the treatment of CTO in the KAMIR population, which limits the comparison and interpretation of the diverging results.

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REPLY: Revascularization Strategies in Patients With Acute MI and Cardiogenic Shock

We thank Dr. de Waha and colleagues for their interest in our study (1). Although most of their comments were rational and valuable, we do not fully agree with their opinions.

They noted potential selection bias of lower risk patients, especially in the multivessel percutaneous coronary intervention (PCI) group. Because our study (1) was not a randomized trial, the revascularization strategy was left to the operators' discretion, which might result in an inherent bias. However, the risk of patient-oriented composite outcome was significantly lower in the "immediate" multivessel PCI group (n = 157) than in the infarct-related artery (IRA)-only PCI group (n = 359) (33.8% vs. 42.6%; inverse probability weight-adjusted hazard ratio: 0.704; 95% CI: 0.528 to 0.939; p = 0.017). Furthermore, patients might have undergone staged PCI for non-IRA lesions due to delayed recovery from cardiogenic shock (CS).

For the second issue, mortality and the rate of renal replacement, as well as study outcomes between our study and the CULPRIT-SHOCK (Culprit Lesion Only PCI Versus Multivessel PCI in Cardiogenic Shock) trial, cannot be directly compared because the study population was different. The Korea Acute Myocardial Infarction Registry (KAMIR)-National Institutes of Health (NIH) registry was a separate registry supported by the NIH and started after the completion of enrollment for the previous KAMIR registries. We reported that multivessel PCI could not reduce mortality in patients with CS complicating ST-segment elevation myocardial infarction and multivessel disease in 2014. For that study, we analyzed patients enrolled in the KAMIR registry between November 2005 and September 2010. In the present study (1), we analyzed patients enrolled in the KAMIR-NIH registry between November 2011 and December 2015. There are substantial differences between the 2 analyses such as stent type (first-generation vs. second-generation drug-eluting stents) and introduction of new potent $P2Y_{12}$ inhibitors in the Republic of Korea.

Regarding the definition of groups, all previous trials that compared complete revascularization versus IRA-only PCI consistently showed the superiority of complete revascularization and classified staged non-IRA PCI as multivessel PCI or complete revascularization (2–5), except the CULPRIT-SHOCK trial. The term "IRA-only PCI with possible staged revascularization" might cause confusion in comparisons with previous trials. Further study is strongly warranted to clarify this issue in patients with acute myocardial infarction presenting with CS.

In terms of the chronic total occlusion issue, the KAMIR-NIH registry did not collect detailed information about detailed procedural characteristics of